

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (original) An oligonucleotide-negatively charged minor groove binder conjugate comprising:
a negatively charged minor groove binder moiety comprising:
at least one aryl moiety, and
at least one acidic moiety capable of ionizing under physiological conditions, wherein said acidic moiety is covalently attached to at least one of said aryl moiety and optionally comprises an acidic moiety linker; and
an oligonucleotide moiety which is covalently attached to said negatively charged minor groove binder moiety.
2. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1, wherein said negatively charged minor groove binder moiety is covalently attached to 3'-position, 5'-position or an internal sugar moiety of said oligonucleotide.
3. (withdrawn) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1, wherein said negatively charged minor groove binder moiety is covalently attached to a heterocyclic base portion of said oligonucleotide moiety.
4. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1, wherein said negatively charged minor groove binder moiety comprises a plurality of said acidic moieties.

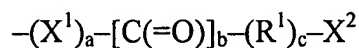
5. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 4, wherein said negatively charged minor groove binder moiety comprises at least three of said acidic moieties.

6. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1, wherein said oligonucleotide comprises from about 3 to about 100 nucleotide units.

7. (withdrawn) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1, wherein at least one of said acidic moiety is covalently attached to at least one of said aryl moiety through said acidic moiety linker.

8. (withdrawn) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 7, wherein said acidic moiety linker comprises from 1 to about 30 atoms selected from the group consisting of C, N, O, S, P and a combination thereof.

9. (withdrawn) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 8, wherein the combination of said acidic moiety and said acidic moiety linker is of the formula:



wherein

each of a, b and c is independently 0 or 1;

each X^1 is independently selected from the group consisting of:

- (i) O,
- (ii) NR^2 , where each R^2 is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl and a nitrogen protecting group, and
- (iii) alkylene;

each R^1 is independently selected from the group consisting of alkylene, cycloalkylene, arylene and a combination thereof; and
each X^2 is independently said acid moiety.

10. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1, wherein said acidic moiety has pKa of about 6 or less.

11. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 10, wherein each of said acidic moiety is independently selected from the group consisting of:

- (i) $-(O)_dS(O)_eOH$, wherein d 0 or 1 and e is 1 or 2, and
- (ii) $-(O)_fP(O)_g(OR^{al})_h(OH)_i$, wherein each R^{al} is independently selected from the group consisting of alkyl, aralkyl and aryl; f is 0 or 1; each of g and h is independently 0, 1, or 2; and i is 1, 2 or 3, provided the sum of g+h+i is 2 or 3;
- (iii) $-CO_2H$; and
- (iv) salts thereof.

12. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1, wherein said acidic moiety is covalently attached to a phenyl moiety or a heteroatom of a heteroaryl portion of said aryl moiety, optionally through said acidic moiety linker.

13. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 12, wherein said aryl moiety of negatively charged minor groove binder is selected from the group consisting of phenyl, a heteroaryl, a fused phenyl-heteroaryl, a fused heteroaryl-phenyl-heterocyclyl and a combination thereof.

14. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1 further comprising a first linker moiety, wherein said negatively charged minor groove binder moiety is covalently attached to said oligonucleotide moiety through said first linker moiety.

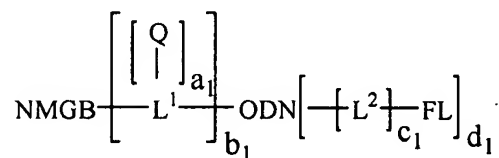
15. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 14 further comprising a quencher moiety, wherein said quencher moiety is covalently attached to said first linker moiety.

16. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 15, wherein said quencher moiety has an absorbance maximum of from about 400 nm to about 1000 nm.

17. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1 further comprising a fluorophore moiety covalently attached to said oligonucleotide moiety, wherein said fluorophore moiety is covalently attached to said oligonucleotide moiety through an optional second linker moiety.

18. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 17, wherein the emission wavelength of said fluorophore moiety is from about 400 to about 1000 nm.

19. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 1 of the formula:



wherein

NMGB is said negatively charged minor groove binder;

ODN is said oligonucleotide;

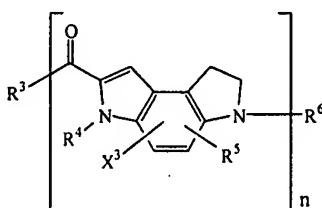
FL is a fluorophore;

Q is a quencher;

L¹ is a first linker comprising a chain of from 3 to about 100 atoms selected from the group consisting of C, N, O, S, P and combinations thereof;

L² is a second linker comprising a chain of from 1 to about 30 atoms selected from the group consisting of C, N, O, S, P and combinations thereof; and each of a₁, b₁, c₁ and d₁ is independently 0 or 1.

20. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 19, wherein NMGB moiety is of the formula:

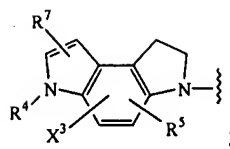


wherein

n is an integer from 2 to 10;

R³ is selected from the group consisting of:

- (a) alkoxy,
- (b) aryloxy,
- (c) R^a-O-L³-N(R^b)-, where L³ is a third linker comprising a chain of from 3 to 20 atoms selected from the group consisting of C, N, O, S, P and combinations thereof; and R^a is hydrogen, a hydroxyl protecting group or attached to L¹; and R^b is hydrogen, alkyl, cycloalkyl or a nitrogen protecting group,
- (d) a moiety of the formula:



where

each of X^3 is independently selected from the group consisting of hydrogen, alkyl, alkoxy, halide, cyano, nitro, the acidic moiety optionally comprising an acidic linker and $-NR^{b1}-C(=O)R^c$, where each R^{b1} is hydrogen, alkyl, cycloalkyl or a nitrogen protecting group, each R^c is independently selected from the group consisting of hydrogen, alkyl, and cycloalkyl;

each of R^4 is independently selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) the acidic moiety optionally comprising an acidic moiety linker,
- (d) $-C(=O)-R^{71}$, where R^{71} is hydrogen, alkyl, hydroxy or alkoxy,
- (e) $-NR'R''$, where each of R' and R'' is independently hydrogen or alkyl, and
- (f) $-(alkylene)-OR^{72}$, where R^{72} is hydrogen or alkyl,

each R^5 is independently selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) alkoxy,
- (d) cycloalkyl,
- (e) halide,
- (f) cyano,
- (g) nitro,
- (h) $-[X^4]_{m1}-C(=O)-[O]_{m2}-R^8$, where each $m1$ and $m2$ is independently 0 or 1, X^4 is O, NR^{b1} , where R^{b1} is hydrogen, alkyl,

cycloalkyl or a nitrogen protecting group and R^8 is hydrogen, alkyl or cycloalkyl, provided when m_2 is 1, R^8 is alkyl or cycloalkyl, and

- (i) $-C(=O)-NR^eR^f$, where each of R^e and R^f is independently hydrogen, alkyl, cycloalkyl and a nitrogen protecting group,
- (j) the acidic moiety optionally comprising an acidic moiety linker,
- (k) $-NR'R''$, where each of R' and R'' is independently hydrogen or alkyl, and
- (l) $-(alkylene)-OR^{72}$, where R^{72} is hydrogen or alkyl;

each of R^6 and R^7 is selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) cycloalkyl,
- (d) $-L^x-Z^x$, where L^x is a linker comprising from 3 to 20 atoms selected from the group consisting of C, N, O, S, P and combinations thereof; Z^x is hydrogen, a protecting group, a solid support or a point of attachment to said first linker L^1 ,
- (e) the acidic moiety optionally comprising an acidic moiety linker, and
- (f) a moiety of the formula $-(Z^1)_j-C(=O)-(R^{10})_k-[C(=O)]_l-R^{11}$,

where

each of j , k and l is independently 0 or 1;

each Z^1 is independently selected from the group consisting of O, NR^{12} and alkylene;

each R^{10} is independently selected from the group consisting of alkylene and cycloalkylene;

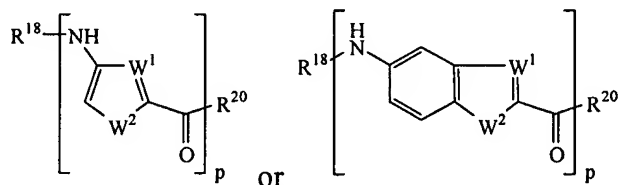
each R^{11} is independently selected from the group consisting of alkyl, alkoxy, aryloxy, $-NR^{13}R^{14}$, $-NR^{15}-NR^{16}R^{17}$, hydroxyalkyl and thioalkyl; and

each of R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and R^{17} is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl and a nitrogen protecting group;

- (g) $-NR'R''$, where each of R' and R'' is independently hydrogen or alkyl;
- (h) $-(alkylene)-OR^{72}$, where R^{72} is hydrogen or alkyl; and
- (i) $-CHO$,

provided at least one of X^3 , R^4 , R^6 , or R^7 comprises said acidic moiety optionally comprising said acidic moiety linker, and provided that one of R^3 , R^6 , R^7 and R^a is a point of attachment to said first linker L^1 .

21. (withdrawn) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 19, wherein NMGB moiety is of the formula:



wherein

W^1 is N or CR^{x30} , where R^{x30} is hydrogen, alkyl, or hydroxy;

W^2 is NR^{19} , S or O;

p is an integer from 2 to 12;

each R^{19} is independently selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) a nitrogen protecting group, and
- (b) said acidic moiety optionally comprising an acidic moiety linker;

each of R^{18} and R^{20} is independently selected from the group consisting of:

- (a) hydrogen,

- (b) alkyl,
- (c) cycloalkyl,
- (d) said acidic moiety; and
- (e) $-(Z^1)_j-C(=O)-(R^{10})_k-[C(=O)]_l-R^{11}$,

where

each of j, k and l is independently 0 or 1;

each Z^1 is independently selected from the group consisting of O,
 NR^{12} and alkylene;

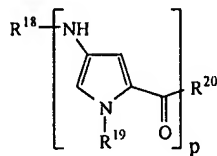
each R^{10} is independently selected from the group consisting of
alkylene and cycloalkylene;

each R^{11} is independently selected from the group consisting of
alkyl, alkoxy, aryloxy, $-NR^{13}R^{14}$, $-NR^{15}-NR^{16}R^{17}$,
hydroxyalkyl and thioalkyl; and

each of R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and R^{17} is independently selected
from the group consisting of hydrogen, alkyl, cycloalkyl
and a nitrogen protecting group;

provided at least one of R^{18} , R^{19} or R^{20} is said acidic moiety, optionally comprising said acidic
moiety linker, and provided that one of R^{18} and R^{20} is a point of attachment to said first linker L^1 .

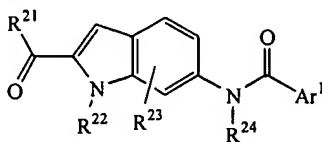
22. (withdrawn) The oligonucleotide-negatively charged minor groove binder
conjugate according to Claim 21, wherein NMGB moiety is of the formula:



wherein

p, R^{18} , R^{19} and R^{20} are those defined in Claim 21.

23. (withdrawn) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 19, wherein NMGB moiety is of the formula:



wherein

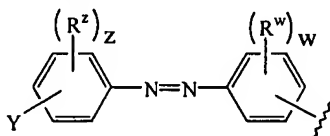
R^{21} is an optionally substituted aryl-heterocyclyl;

each of R^{22} and R^{24} is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl and a nitrogen protecting group;

Ar^1 is optionally substituted aryl moiety; and

R^{23} is selected from the group consisting of hydrogen and said acidic moiety optionally comprising said acidic moiety linker, provided when R^{23} is hydrogen at least one of Ar^1 or R^{21} is substituted with said acidic moiety optionally comprising said acidic moiety linker, and provided that one of R^{21} , R^{22} , R^{23} and R^{24} is a point of attachment to said first linker L^1 .

24. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 19, wherein said quencher moiety, Q, is of the formula:



wherein

Y is selected from the group consisting of substituted phenyldiazenyl, nitro and $-NR^{50}R^{51}$, where each of R^{50} and R^{51} is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl and a nitrogen protecting group;

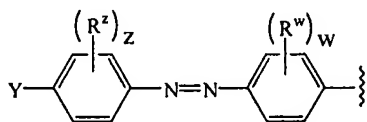
each of z and w is independently an integer from 0 to 4;

each R^z is independently selected from the group consisting of hydrogen, nitro, cyano, halide and $-S(O)_{aa}NR^{52}R^{53}$, where aa is 0, 1 or 2 and each of R^{52} and R^{53} is independently

selected from the group consisting of hydrogen, alkyl, cycloalkyl and a nitrogen protecting group, or two adjacent R^z's and carbon atom to which they are attached to forms a five- or six-membered ring having from zero to three heteroatoms as ring members; and

each R^w is independently selected from the group consisting of alkoxy, halide and -NR⁵⁴-C(=O)R⁵⁵, where R⁵⁴ is selected from the group consisting of hydrogen, alkyl and a nitrogen protecting group, and R⁵⁵ is selected from the group consisting of hydrogen, alkyl and cycloalkyl, or two adjacent R^w's and carbon atom to which they are attached to forms a five- or six-membered ring having from zero to three heteroatoms as ring members.

25. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 24, wherein said quencher moiety is of the formula:

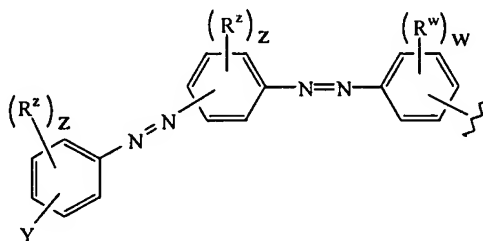


wherein

w, z, R^w and R^z are those defined in Claim 24; and

Y is selected from the group consisting of nitro and -N(CH₃)₂.

26. (withdrawn) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 24, wherein said quencher moiety is of the formula:



wherein

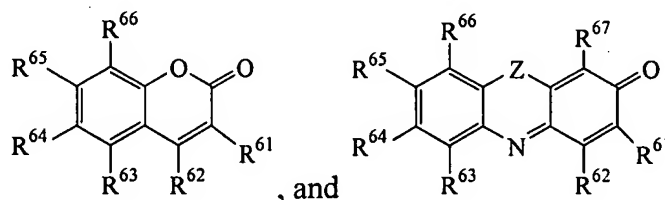
Y is selected from the group consisting of nitro and -NR⁵⁰R⁵¹; and

w, z, R^w, R^z, R⁵⁰ and R⁵¹ are those defined in Claim 24.

27. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 19, wherein said fluorophore has emission wavelength of from about 400 to about 1000 nm.

28. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 27, wherein said fluorophore, FL, is selected from the group consisting of a derivative of fluoresceine, cyanine, resorufin and coumarin.

29. (withdrawn) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 28, wherein said fluorophore, FL, is a coumarin derivative selected from the group consisting of:



wherein

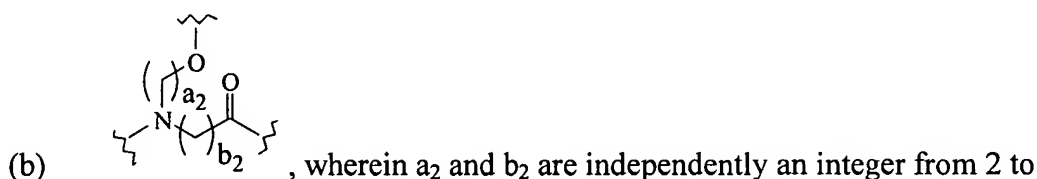
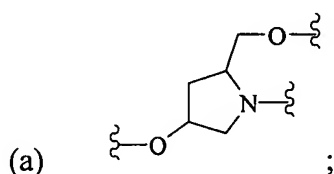
each of R^{61} , R^{62} , R^{63} , R^{64} , R^{65} , R^{66} and R^{67} is independently selected from the group consisting of hydrogen, halide, nitro, cyano, $-\text{SO}_3R^{70}$, $-\text{SO}_2\text{N}(R^{70})_2$, $-\text{C}(=\text{O})\text{OR}^{70}$, $-\text{C}(=\text{O})\text{N}(R^{70})_2$, $-\text{CNS}$, $-\text{OR}^{70}$, $-\text{OC}(=\text{O})R^{70}$, $-\text{SR}^{70}$, $-\text{NHC}(\text{O})R^{70}$, $-\text{CF}_3$, $-\text{N}(R^{70})_2$, wherein each R^{70} is independently selected from the group consisting of hydrogen, $\text{C}_1\text{-C}_8$ alkyl, aryl and a protecting group compatible with oligonucleotide synthesis, or

two adjacent groups of R^{61} through R^{66} together with the carbon atoms to which they are attached form a five- or six-membered ring having from zero to three heteroatoms as ring member; and

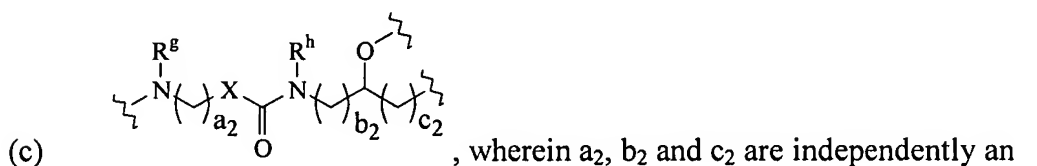
Z is O or S;

provided that at least one of R^{61} through R^{67} is a point of attachment to said second linker L^2 or to said oligonucleotide ODN.

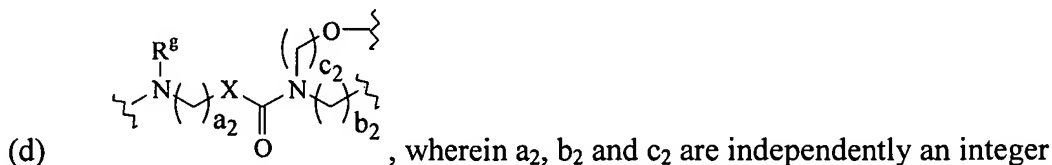
30. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 19, wherein L^1 comprises a moiety selected from the group consisting of:



10;

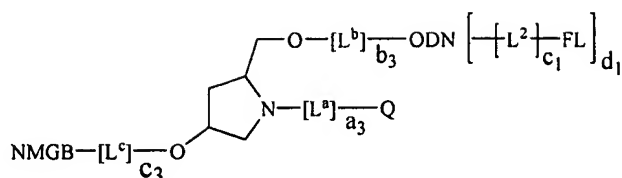


, wherein a_2 , b_2 and c_2 are independently an integer from 2 to 10, X is O, CH_2 or NR^i and each of R^g , R^h and R^i is independently hydrogen, alkyl, cycloalkyl or a nitrogen protecting group; and



, wherein a_2 , b_2 and c_2 are independently an integer from 2 to 10, X is O, CH_2 or NR^i and each of R^g and R^i is independently hydrogen, alkyl, cycloalkyl or a nitrogen protecting group.

31. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 30 of the formula:



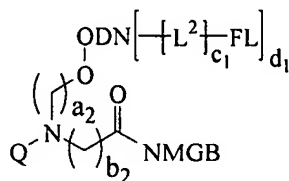
wherein

c_1 , d_1 , L^2 , Q, ODN, NMGB and FL are those defined in Claim 19;

each of a_3 , b_3 and c_3 is 0 or 1; and

each of L^a , L^b and L^c is independently a linker comprising an acyclic chain of from 1 to about 10 atoms, wherein each atom of the acyclic chain is independently selected from the group consisting of C, N, O, S and P.

32. (original) The oligonucleotide-negatively charged minor groove binder conjugate according to Claim 30 of the formula:



wherein

c_1 , d_1 , L^2 , FL, Q, ODN and NMGB are those defined in Claim 19; and

a_2 and b_2 are those defined in Claim 30.

33. (withdrawn) A negatively charged minor groove binding compound comprising a binding moiety that binds preferentially into a minor groove of a double stranded oligonucleotide, wherein said binding moiety comprises:

at least one aryl moiety, and

at least one acidic moiety capable of ionizing under physiological conditions,

wherein said acidic moiety is covalently attached to a phenyl moiety of said aryl moiety or a

heteroatom of a heteroaryl portion of said aryl moiety, wherein said acidic moiety optionally comprises an acidic moiety linker.

34. (withdrawn) The negatively charged minor groove binding compound according to Claim 33, wherein said aryl moiety is selected from the group consisting of phenyl, a heteroaryl, a fused phenyl-heteroaryl, a fused heteroaryl-phenyl-heterocyclyl and a combination thereof.

35. (withdrawn) The negatively charged minor groove binding compound according to Claim 33, wherein said acid moiety has pKa of about 6 or less.

36. (withdrawn) The negatively charged minor groove binding compound according to Claim 33, wherein said binding moiety comprises a plurality of aryl moieties.

37. (withdrawn) The negatively charged minor groove binding compound according to Claim 36, wherein said binding moiety comprises at least three aryl moieties.

38. (withdrawn) The negatively charged minor groove binding compound according to Claim 36, wherein each of said aryl moiety is independently selected from the group consisting of indole, benzofuran, pyrroloindole, hydropyrroloindole, phenyl, pyrrole, benzimidazole, imidazole, pyridine, 6-phenylimidazo[4,5-b]pyridine, furan, thiazole and oxazole.

39. (withdrawn) The negatively charged minor groove binding compound according to Claim 36 comprising a plurality of said acidic moieties.

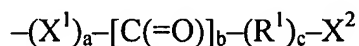
40. (withdrawn) The negatively charged minor groove binding compound according to Claim 39 comprising at least three of said acidic moieties.

41. (withdrawn) The negatively charged minor groove binding compound according to Claim 33, wherein each of said acidic moiety is independently selected from the group consisting of:

- (i) $-(O)_dS(O)_eOH$, wherein d is 0 or 1 and e is 1 or 2, and
- (ii) $-(O)_fP(O)_g(OR^{al})_h(OH)_i$, wherein each R^{al} is independently selected from the group consisting of alkyl, aralkyl and aryl; f is 0 or 1; each of g and h is independently 0, 1, or 2, and i is 1, 2 or 3, provided the sum of g+h+i is 2 or 3;
- (iii) $-CO_2H$; and
- (iv) salts thereof.

42. (withdrawn) The negatively charged minor groove binding compound according to Claim 41 further comprising said acidic moiety linker, wherein said acidic moiety linker comprises from 1 to about 20 atoms selected from the group consisting of C, N, O, S, P and combinations thereof.

43. (withdrawn) The negatively charged minor groove binding compound according to Claim 42, wherein the combination of said acidic moiety and said acidic moiety linker is of the formula:



wherein

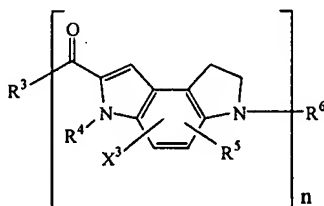
each of a, b and c is independently 0 or 1, provided at least one of b and c is 1;
each X^1 is independently selected from the group consisting of:

- (i) O,
- (ii) NR^2 , where each R^2 is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, and a nitrogen atom protecting group, and
- (iii) alkylene;

each R^1 is independently selected from the group consisting of alkylene, cycloalkylene, arylene and a combination thereof; and
 X^2 is said acid moiety.

44. (withdrawn) The negatively charged minor groove binding compound according to Claim 41, wherein X^2 is selected from the group consisting of $-\text{SO}_2\text{OH}$, $-\text{OPO}_2(\text{OH})$, $-\text{CO}_2\text{H}$, and salts thereof.

45. (withdrawn) The negatively charged minor groove binding compound according to Claim 38 of the formula:

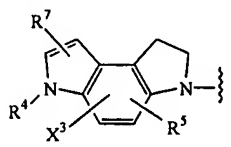


wherein

n is an integer from 2 to 10;

R^3 is selected from the group consisting of:

- (a) alkoxy,
- (b) aryloxy,
- (c) $R^a-\text{O}-\text{L}^3-\text{NR}^b-$, where R^a is hydrogen or a hydroxyl protecting group; R^b is hydrogen, alkyl, cycloalkyl or a nitrogen protecting group, and L^3 is a linker comprising a chain of from 3 to 20 atoms selected from the group consisting of C, N, O, S, P and combinations thereof, and
- (d) a moiety of the formula:



each R^4 is independently hydrogen, alkyl or said acidic moiety, optionally comprising said acidic moiety linker;

each X^3 is independently selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) alkoxy,
- (d) halide,
- (e) cyano,
- (f) nitro,
- (g) $-NR^{b1}-C(=O)-R^c$, where R^{b1} is hydrogen, alkyl, cycloalkyl or a nitrogen protecting group and R^c is hydrogen, alkyl or cycloalkyl, and
- (h) said acidic moiety, optionally comprising said acidic moiety linker;

each R^5 is independently selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) alkoxy,
- (d) cycloalkyl,
- (e) halide,
- (f) cyano,
- (g) nitro,
- (h) $-[X^4]_{m1}-C(=O)-[O]_{m2}-R^8$, where each $m1$ and $m2$ is independently 0 or 1, X^4 is O, NR^{b1} , where R^{b1} is hydrogen, alkyl, cycloalkyl or a nitrogen protecting group and R^8 is hydrogen, alkyl or cycloalkyl, provided when $m2$ is 1, R^8 is alkyl or cycloalkyl, and
- (i) $-C(=O)-NR^eR^f$, where each of R^e and R^f is independently hydrogen, alkyl, cycloalkyl and a nitrogen protecting group, and
- (j) said acidic moiety, optionally comprising said acidic moiety linker;

each of R^6 and R^7 is independently selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) cycloalkyl,
- (d) $-L^xZ^x$, where L^x is a linker comprising from 3 to 20 atoms selected from the group consisting of C, N, O, S, P and combinations thereof, and Z^x is selected from the group consisting of hydrogen, a protecting group or a solid support,
- (f) a moiety of the formula $-(Z^1)_j-C(=O)-(R^{10})_k-[C(=O)]_l-R^{11}$,

where

each of j , k and l is independently 0 or 1;

each Z^1 is independently selected from the group consisting of O,
 NR^{12} and alkylene;

each R^{10} is independently selected from the group consisting of
alkylene and cycloalkylene;

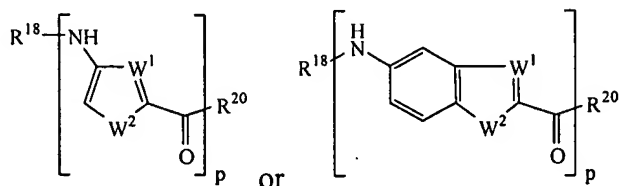
each R^{11} is independently selected from the group consisting of
alkyl, alkoxy, aryloxy, $-NR^{13}R^{14}$, $-NR^{15}-NR^{16}R^{17}$,
hydroxyalkyl and thioalkyl; and

each of R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and R^{17} is independently selected
from the group consisting of hydrogen, alkyl, cycloalkyl
and a nitrogen protecting group; and

(f) said acidic moiety optionally comprising said acidic moiety linker;
provided at least one of X^3 , R^4 , R^6 and R^7 is said acidic moiety optionally comprising said acidic
moiety linker.

46. (withdrawn) The negatively charged minor groove binding compound
according to Claim 45, wherein n is 2 to 8.

47. (withdrawn) The negatively charged minor groove binding compound according to Claim 38 of the formula:



wherein

W^1 is N or CR^{x30} , where R^{x30} is hydrogen, alkyl, or hydroxy;

W^2 is NR^{19} , S or O;

p is an integer from 2 to 12;

each R^{19} is independently selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) a nitrogen protecting group, and
- (b) said acidic moiety optionally comprising an acidic moiety linker;

each of R^{18} and R^{20} is independently selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) cycloalkyl,
- (d) said acidic moiety; and
- (e) $-(Z^1)_j-C(=O)-(R^{10})_k-[C(=O)]_l-R^{11}$,

where

each of j, k and l is independently 0 or 1;

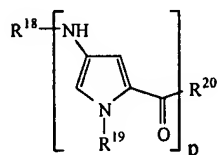
each Z^1 is independently selected from the group consisting of O,

NR^{12} and alkylene;

each R^{10} is independently selected from the group consisting of
alkylene and cycloalkylene;

each R^{11} is independently selected from the group consisting of
alkyl, alkoxy, aryloxy, $-NR^{13}R^{14}$, $-NR^{15}-NR^{16}R^{17}$,
hydroxyalkyl and thioalkyl; and
each of R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and R^{17} is independently selected
from the group consisting of hydrogen, alkyl, cycloalkyl
and a nitrogen protecting group;
provided at least one of R^{18} , R^{19} or R^{20} is said acidic moiety, optionally comprising said acidic
moiety linker.

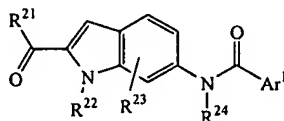
48. (withdrawn) The negatively charged minor groove binding compound
according to Claim 47 of the formula:



wherein

p , R^{18} , R^{19} and R^{20} are those defined in Claim 47.

49. (withdrawn) The negatively charged minor groove binding compound
according to Claim 38 of the formula:



wherein

R^{21} is an optionally substituted aryl-heterocyclyl;

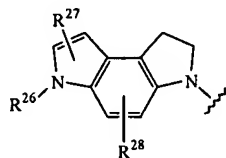
each of R^{22} and R^{24} is independently selected from the group consisting of
hydrogen, alkyl, and a nitrogen protecting group;

Ar^1 is optionally substituted aryl moiety; and

R^{23} is selected from the group consisting of hydrogen and said acidic moiety, optionally comprising said acidic moiety linker; provided when R^{23} is hydrogen at least one of Ar^1 or R^{21} is substituted with said acidic moiety, optionally comprising said acidic moiety linker.

50. (withdrawn) The negatively charged minor groove binding compound according to Claim 49, wherein R^{22} and R^{24} are hydrogen.

51. (withdrawn) The negatively charged minor groove binding compound according to Claim 50, wherein R^{21} is selected from the group consisting of:



wherein

R^{26} is selected from the group consisting of hydrogen, alkyl, and a nitrogen protecting group;

R^{27} is selected from the group consisting of:

- (a) hydrogen,
- (b) alkyl,
- (c) cycloalkyl,
- (d) said acidic moiety, optionally comprising said acidic moiety linker,
- (e) $-(Z^1)_j-C(=O)-(R^{10})_k-[C(=O)]_l-R^{11}$,

where

each of j , k and l is independently 0 or 1;

each Z^1 is independently selected from the group consisting of O, NR^{12} and alkylene;

each R^{10} is independently selected from the group consisting of alkylene and cycloalkylene;

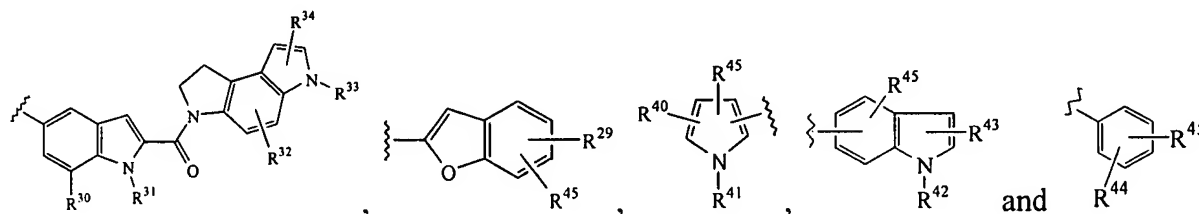
each R^{11} is independently selected from the group consisting of
alkyl, alkoxy, aryloxy, $-NR^{13}R^{14}$, $-NR^{15}-NR^{16}R^{17}$,
hydroxyalkyl and thioalkyl; and

each of R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and R^{17} is independently selected
from the group consisting of hydrogen, alkyl, cycloalkyl,
and a nitrogen protecting group, and

- (f) $-L^xZ^x$, where L^x is a linker comprising from 3 to 20 atoms selected
from the group consisting of C, N, O, S, P and combinations
thereof, and Z^x is selected from the group consisting of hydrogen, a
protecting group or a solid support; and

R^{28} is selected from the group consisting of hydrogen and said acidic moiety optionally
comprising said acidic moiety linker.

52. (withdrawn) The negatively charged minor groove binding compound
according to Claim 50, wherein Ar^1 is selected from the group consisting of:



wherein

each of R^{29} , R^{30} and R^{32} is independently selected from the group consisting of
hydrogen and said acidic moiety, optionally comprising said acidic moiety linker;

R^{34} is selected from the group consisting of:

- hydrogen,
- alkyl,
- cycloalkyl,
- said acidic moiety, optionally comprising said acidic moiety linker,
- $-(Z^1)_j-C(=O)-(R^{10})_k-[C(=O)]_l-R^{11}$,

where

each of j, k and l is independently 0 or 1;

each Z^1 is independently selected from the group consisting of O,
 NR^{12} and alkylene;

each R^{10} is independently selected from the group consisting of
alkylene and cycloalkylene;

each R^{11} is independently selected from the group consisting of
alkyl, alkoxy, aryloxy, $-NR^{13}R^{14}$, $-NR^{15}-NR^{16}R^{17}$,
hydroxyalkyl and thioalkyl; and

each of R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , and R^{17} is independently selected
from the group consisting of hydrogen, alkyl, cycloalkyl,
and a nitrogen protecting group, and

(f) $-L^xZ^x$, where L^x is a linker comprising from 3 to 20 atoms selected
from the group consisting of C, N, O, S, P and combinations
thereof, and Z^x is selected from the group consisting of hydrogen, a
protecting group or a solid support;

each of R^{31} and R^{33} is independently selected from the group consisting of
hydrogen, alkyl, a nitrogen protecting group and said acidic moiety optionally comprising an
acidic moiety linker;

each of R^{40} , R^{43} and R^{44} is independently selected from the group consisting of
hydrogen, alkyl, and a moiety of the formula $-L^xZ^x$, $-(Z^1)_j-C(=O)-(R^{10})_k-[C(=O)]_l-R^{11}$;

each of R^{41} and R^{42} is independently selected from the group consisting of
hydrogen, alkyl, and said acidic moiety which optionally comprises said acidic moiety linker;
and

R^{45} is selected from the group consisting of hydrogen, alkyl, alkoxy, cycloalkyl,
halide, cyano, nitro, and a moiety of the formula $-[X^4]_{m1}-C(=O)-[O]_{m2}-R^8$, wherein each of m1
and m2 is independently 0 or 1, X^4 is O, NR^{b1} , where R^{b1} is hydrogen, alkyl, cycloalkyl or a
nitrogen protecting group and R^8 is hydrogen, alkyl or cycloalkyl, provided when m2 is 1, R^8 is
alkyl or cycloalkyl.

53. (original) The negatively charged minor groove binding compound according to Claim 33, wherein said negatively charged minor groove binding compound is covalently attached to a solid support.

54. (withdrawn) The negatively charged minor groove binding compound according to Claim 53, wherein said negatively charged minor groove binding compound is attached to said solid support through a solid support linker.

55. (withdrawn) A method for identifying a nucleic acid comprising:
- (a) incubating a first oligonucleotide with an oligonucleotide probe; and
 - (b) identifying a hybridized nucleic acid;

wherein said oligonucleotide probe comprises:

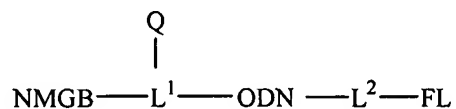
a negatively charged minor groove binder moiety comprising:

at least one aryl moiety, and

at least one acidic moiety capable of ionizing under physiological conditions, wherein said acidic moiety is covalently attached to at least one of said aryl moiety, optionally through an acidic moiety linker; and

an oligonucleotide moiety which is covalently attached to said negatively charged minor groove binder moiety.

56. (withdrawn) The method of Claim 55, wherein said oligonucleotide probe is of the formula:



wherein

NMGB is said negatively charged minor groove binder;

ODN is said oligonucleotide;

FL is a fluorophore;

Q is a quencher;

L¹ is a first linker comprising from 3 to about 100 atoms selected from the group consisting of C, N, O, S, P and combinations thereof; and

L² is a second linker comprising from 1 to about 30 atoms selected from the group consisting of C, N, O, S, P and combinations thereof.

57. (original) A pharmaceutical composition comprising an oligonucleotide-negatively charged minor groove binder conjugate of Claim 1.

58. (withdrawn) A method for inhibiting gene expression in a cell comprising administering an oligonucleotide-negatively charged minor groove binder conjugate of Claim 1 to the cell.

59. (withdrawn) A method for inhibiting DNA replication in a cell comprising administering an oligonucleotide-negatively charged minor groove binder conjugate of Claim 1 to the cell.

60. (withdrawn) A method for treating cancer in a patient comprising administering to the patient a therapeutically effective amount of an oligonucleotide-negatively charged minor groove binder conjugate of Claim 1.

61. (withdrawn) The method of Claim 60, wherein said cancer is selected from carcinoma of the bladder, melanoma, and lung cancer.

62. (withdrawn) A method for treating viral infection in a patient comprising administering to the patient a therapeutically effective amount of an oligonucleotide-negatively charged minor groove binder conjugate of Claim 1.

63. (withdrawn) The method of Claim 62, wherein the viral infection is HIV infection.